REMARKS

The allowance of claim 14 is acknowledged. The indication that the subject matter of claim 2 would be allowable is likewise acknowledged, and claim 2 has now been canceled and incorporated into claim 1. The indication that claim 23 would be allowable is further acknowledged, and the subject matter of claim 23 has now been incorporated into claim 22. Accordingly, it is believed that independent claims 1, 14 and 22, and the claims dependent thereupon, should now be allowed.

The rejection under 35 USC § 112 second paragraph has been considered and claim 1 has been amended in a manner which is believed to cure those objections. Accordingly, it is believed that this Section 112 rejection should now be withdrawn.

The remaining rejections of independent claims 15 and 25 and dependent claim 16 under 35 U.S.C. § 103(a) based upon the Korean IPO Publication No. 10-2000-0072201 (hereinafter "Kim") in view of the disclosure of U.S. Patent No. 6,268,147 to Beattie et al. (hereinafter "Beattie et al.") in view of O'Connell et al (Clinical Genetics, Vol. 61, p. 13-20, 2002) (hereinafter "O'Connell et al"), and further in view of U.S. Patent No. 5,753,439 to Smith et al (hereinafter Smith et al) are respectfully traversed. The subject matter of independent claims 15 and 25 would not be obvious from the disclosure of Kim, as potentially modified by the disclosures of Beattie et al., O'Connell et al and Smith et al.

Kim proposes a method for diagnosing fragile X syndrome using DNA probes wherein the results of Kim's efforts are all cumulatively injected into a microwell plate

so as to become attached to the streptavidin coating in the well. This is Kim's improvement over Southern Blotting.

O'Connell et al simply employ the tradition method of determining nucleic acid length, namely electrophoresis (see page 140).

Whereas it is true that Beattie et al and Smith et al show the use of microarrays, both are far different than Applicant's microarray, and neither would be usable to effect analysis of the products of Kim. They are two different alternative solutions to the solution that Kim proposes.

Smith et al propose a totally different concept that would be an alternative to the Kim teaching. As pointed out in Example 4 at column 12, lines 35-38, they would synthesize 100 different target nucleic acid probes varying from 10-109 internal repeats and arrange them in an array of 10-by-10. They would then hybridize the targets to this array and look for the "perfect match" (see column 8, lines 41-58). It should be quite apparent that such a practice would be a clear alternative to the teachings of both Kim and Applicant and not something that would be additive to or useful with either's process.

Beattie et al similarly uses another alternative process which employs the use of labeled stacking probes. These labeled stacking probes each contain a unique sequence on one side of an STRP plus a set number of repeat units. A hybrid of such a tandem probe and nucleic acid being diagnosed will only, very specifically bind to a capture probe attached to a microarray. Binding of target nucleic acid hybrid will only occur when it is hybridized in tandem with one such labeled stacking probe so as to form

contiguously stacked labeled probe/capture probe duplex structures. Accordingly, this Beattie et al. technique uses tandem or duplex targets that respectively contain nucleic acid complementary to a portion of the region of interest and a contiguous DNA sequence that flanks the region of interest. When the arrangement is used to detect STRP, as illustrated, for example, in FIG. 14B, there must be precise registration between two such duplex targets/probes. Where the marker contains 10 repeat units, for example, a capture probe bearing four repeat units would not stack with a hybrid of a stacking probe bearing four repeat units, i.e. such would require a capture probe bearing six repeat units, see column 37, lines 47-62. Only one signal from the correctly hybridized probes is then detected as part of the analysis.

Applicant's method of invention for detection is quite different from the disclosure of Beattie et al. Applicant employs two sets of different, labeled, oligonucleotide targets; Applicant separately targets (i) CGG repeats and (ii) the contiguous nucleic acid segment and then separately sequesters these in a microarray. Ultimately, following hybridization to the microarray, the colorometric intensities of the separately hybridized target oligonucleotides representing either the CGG repeats or the contiguous nucleic acid segment (which are present at different locations so as not to interfere with one another) are measured and compared to determine the ratio of signal intensity at the CGG repeat probe regions to the signal intensity at the contiguous nucleic acid segment target regions. It is this ratio which is then used for comparison with known control samples to accurately quantify the number of CGG repeats present in the genomic DNA being tested. Thus, Applicant's invention employs the reading of two

separate colorometric intensities and comparing the ratio between those readings with ratios obtained from known control samples, whereas Beattie et al is merely looking for a single intensity that would be indicative of a single mutation or STRP.

As recited in claims 15 and 25, Applicant's invention first reads two separate colorometric intensities and then compares the ratio between those intensity readings to results from known control samples; in this manner Applicant is able to accurately quantify the length of the segment, i.e. the number of STRs, e.g. CGG repeats, in the region of interest of the obtained DNA. Both Smith et al and Beattie et al use highly specialized arrays to generate only a single signal which is indicative of the length of repeats. Moreover, they are both alternative procedures that one would use instead of the Kim procedure and not as a part of it.

In summary, previously electrophoresis has been used to determine nucleic acid length. It is submitted that Applicant's use of a microarray in this manner to obtain an accurate quantification of the number of STRs in a region of interest in DNA by obtaining a ratio of two colorometric intensity signals and comparing the results to similar results from known control samples is not fairly suggested by the prior art, and claims 15 and 25 along with dependent claim 16 should be allowed.

Claim 14 was found allowable and is indicated that claims 1, 3, 5-13, 22 and 24 would now be allowable as a result of the amendments made thereto. In view of the foregoing, it is believed that claims 15, 16 and 25 should also be allowed and that this application has thus been placed in condition for allowance. Favorable action is courteously submitted.

Respectfully submitted,

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